REMARKS

Claims 1-3 and 5-30 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kim.

The Examiner recognizes that Kim does not explicitly teach the osmotic pressure of the disclosed composition, however, it is the Examiner's position that absent evidence to the contrary, or a showing of unexpected results, the claimed osmolarity range is not considered "patentably significant". The Examiner's position with respect to the dependent claims is the same as previously set forth in the Office Action dated June 14, 2001, which is that it would have been obvious to one of ordinary skill in the art to include a hemostatic agent in a mucosal formulation to prevent unwanted bleeding and that it would have been obvious to one of ordinary skill in the art to use any osmotic agent, or water soluble polymer known in the pharmaceutical art to make an aqueous pharmaceutical composition for mucosal administration based upon the teachings of Kim.

In response to the Preliminary Amendment and Declaration of Atsuhiro Nagano, the Examiner states that the arguments and data are not persuasive. Specifically, the Examiner does not find the Declaration to be commensurate in scope with the scope of the claims. The Examiner notes that the Declaration discloses examples of compositions having osmolarities ranging from 90 to 340 mOsm, but the claims recite an osmolarity of 72 mOsm or less.

Further, the Examiner states that the data submitted in the Attachment filed on November 14, 2001, is not commensurate in scope with the scope of the present claims. The Examiner asserts that it appears that osmolarities up to 72 mOsm do not render a significant increase in

bioavailability. The Examiner further asserts that it appears as if an increase in biovailability occurs at an osmolarity between 72 [73] and 30 mOsm but that there is no data between these two limits, so it is not possible to tell where the bioavailability begins to increase unexpectedly.

The Examiner also maintains her position that the difference between 13% and 16% bioavailability does not show an unexpected result compared to the difference between 13% and 47% as shown at page 2 of the Attachment in the first Table comparing 30, 72 and 128 mOsm.

In addition, the Examiner notes that the claims recite a osmolarity of less than 72 mOsm but that the data shows a decrease in bioavailability for compositions having an osmolarity between 5 mOsm and 0 mOsm.

The Examiner also maintains her position that absent evidence to the contrary, the composition of Kim would inherently possess all of the properties of the claimed invention since Kim teaches all of the claimed components.

Applicants respectfully traverse the rejection and the Examiner's statements that the claimed osmolarity range is not "patentably significant" and that the composition of Kim inherently possesses all of the properties of the claimed invention. Applicants have repeatedly indicated that the most important characteristic of the claimed invention is the osmotic pressure of the claimed composition. See, e.g., the Request for Reconsideration filed on August 13, 2001. Thus, it is arbitrary and improper for the Examiner to state that this claimed feature of the invention is insignificant.

Further, Applicants have also explained in the Declaration filed on August 13, 2001, that the closest exemplified example of Kim does not provide an osmolarity below 290 mOsm, much less below 72 mOsm as presently claimed. In fact, in the Declaration, it is indicated that the osmolarity of Example 1 of Kim was measured and determined to be 319 mOsm, which is well above the presently claimed range. The Examiner has not provided any scientific evidence or reasoning to refute the factual determination that the osmolarity of the composition of Kim is 319 mOsm. Thus, the evidence presented is sufficient to establish that Kim does not inherently possess all of the elements of the claimed invention. Applicants respectfully submit that it is improper for the Examiner to summarily dismiss the Declaration as not compelling in this regard. *See* MPEP §2144.08(II)(B) citing *In re Piasecki*, 745 F.2d 1468, 1473 (Fed. Cir. 1984).

With respect to the Examiner's statement that the Declaration of Atsuhiro Nagano, is not commensurate in scope with the scope of the claims because it discloses examples having osmolarities of 90 to 340, which is outside of the claimed range, Applicants note that the Declaration of Atsuhiro Nagano filed on August 13, 2001, in the present application relates only to the osmolarity of the Kim reference as discussed above and does not disclose examples of compositions having osmolarities ranging from 90 to 340 mOsm as stated by the Examiner. A Declaration of Atsuhiro Nagano disclosing examples of compositions having osmolarities ranging from 90 to 340 mOsm was filed in co-pending Application Serial No. 10/201,303, on August 8, 2002, and was not intended for the present application.

In regard to the Examiner's statements regarding the data submitted with the Amendment filed on November 14, 2001, that the Examiner is basing her statement on a comparison of the

increase in bioavailability between compositions disclosed in the present specification instead of between a composition of the claimed invention and the prior art. This is improper. The data referred to in the Table on page 2 of the Attachment to the Amendment filed on November 14, 2001, shows that at an osmolarity of 72 mOsm, bioavailability increases from 7% to 16% when compared to a composition having an osmolarity of 290 mOsm. Thus, at 72 mOsm, there is an increase in bioavailability of at least 9% over the prior art. The data further shows that as the osmolarity is decreased below 72 mOsm, the bioavailability steadily increases. Thus, it follows that a composition of the claimed invention having an osmolarity of less than 72 mOsm would have an even greater increase in bioavailability than the composition having a bioavailability of 72 mOsm, when compared to the prior art. Therefore, the data presented shows a significant increase of greater than 9% in bioavailability, which establishes that the claimed invention provides unexpectedly superior results over the prior art.

With respect to the Examiner's statements regarding the lack of data showing the bioavailability at zero (0) osmolarity, Applicants note that the proper inquiry is whether one of ordinary skill in the art would be able to determine a trend in the data that would allow the artisan to reasonably extend the probative value of the data. In this regard Applicants submit that the osmotic pressure-increasing effect of the water-insoluble or low water soluble substance represented by, for example, crystalline cellulose or Carmellose sodium, is very small, and therefore, usually, to obtain an upper part of the claimed osmotic pressure range (e.g., an osmotic pressure of higher than 10 mOsm and up to 72 mOsm), an osmotic pressure-controlling agent that is a water soluble low molecular weight compound is used, such as sodium chloride,

glucose, etc. However, in the lower part of the claimed osmotic pressure range, such as 0 to 10 mOsm, it is difficult to use the pressure-controlling agent to control the osmotic pressure. Therefore, the osmotic pressure in the lower part of the claimed osmotic pressure range must be controlled by the claimed "water-insoluble and/or lower water soluble substance."

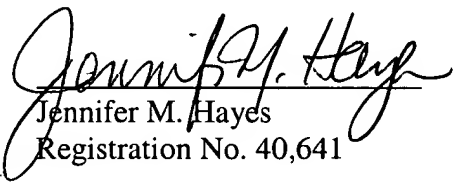
On the other hand, as previously argued, the bioavailability (B.A.) is controlled by the osmotic pressure. However, as known in the art, osmotic pressure is not THE sole factor for determining bioavailability. The kind of solutes and the ratio of the solutes have an effect on bioavailability. In the Table on page 3 of the attachment to the Amendment filed on November 14, 2001, the ratio of crystalline cellulose and Carmellose sodium is not the same between compositions 1, 9 and 8, Therefore, the increase in bioavailability and the decrease in osmotic pressure are not completely parallel. However, this does not negate patentability of the claimed invention, because it is still true that the higher part of the claimed osmotic pressure range, e.g., represented by 72 or 30 mOsm provides a higher bioavailability than that provided by the lower part of the claimed osmotic pressure range, e.g., represented by 5 mOsm, as can be seen in the first and second Tables on page 2 of the attachment to the Amendment filed on November 14, 2001.

Thus, in view of the above, Applicants have established that the claimed invention provides significant unexpectedly superior results, commensurate in scope with the claimed invention, when compared to the prior art. Further, one of ordinary skill in the art would not have had a reasonable expectation of achieving the claimed invention based upon the prior art. Accordingly, Applicants respectfully request withdrawal of the rejection.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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Date: April 8, 2003